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**The hedgehog signalling pathway in the gastrointestinal tract: implications for development, homeostasis, and disease.**

**Lees C, Howie S, Sartor RB, Satsangi J.**

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The hedgehog signalling pathway is critical to normal mammalian gastrointestinal development. Through epithelial-mesenchymal interactions, hedgehog signalling ensures appropriate axial patterning of the embryonic gut. Congenital abnormalities, including malrotations, anorectal malformations, and tracheoesophageal fistula are associated with germ-line mutations/deletion of genes encoding hedgehog signalling components in man and present in genetically engineered animal models. In adults, there is evidence that the pathway plays a role in maintaining stem cell populations in the stomach and directing epithelial cell differentiation in the intestine. Recent data implicate hedgehog signalling in the formation and maintenance of a number of malignancies, including those of the upper gastrointestinal (GI) tract and pancreas, in which abrogation of the pathway offers a novel therapeutic approach in animal models. Most recently, evidence in vitro indicates that there is a recapitulation of embryonic hedgehog signalling in acute epithelial injury and chronic inflammation, a finding with key implications for inflammatory disorders of the intestine, such as inflammatory bowel diseases. This pathway may provide an important link between chronic inflammation and cancer. We summarize the available evidence demonstrating that this developmental pathway has continuing roles in adult homeostasis and is dysregulated in malignancy and inflammation of the gastrointestinal tract.

PMID: 16285967 [PubMed - indexed for MEDLINE]

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